can be extended to telomeric or interstitial rearrangements falling into a size critical for their detection even on high quality chromosome preparations. The setting up of appropriate microarray tests will probably bypass this problem. For the moment, FISH telomere analysis is an excellent support to the clinician faced with a malformed, mentally retarded subject in whom known syndromes have been excluded.

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Laryngeal atresia, encephalocele, and limb deformities (LEL): a possible new syndrome

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EDITOR—In 1987, Machin *et al*¹ reported a case of laryngeal atresia in association with an asymmetrical parietal encephalocele and limbs anomalies. Other anomalies included a horse-shoe kidney and immature, low set ears. We now report a similar case and discuss possible aetiologies and the differential diagnosis.

Case report

This was the second pregnancy of a non-consanguineous, healthy couple with an unremarkable family history; the mother was 26 years old. Ultrasonographic findings at 23 weeks'

gestation were gross fetal ascites and enlarged echogenic lungs subsequently found to be the result of laryngeal atresia (fig 1). There was a large facial cleft with an anterior encephalocele involving the left orbit (fig 1). There were also flexion deformities at the wrists and hips suggesting bilateral radial and tibial aplasia, respectively (fig 1). In view of the serious nature of the anomalies, the parents requested a termination of the pregnancy. Asystole was induced by intracardiac injection of potassium chloride and labour was induced. Analysis of fetal blood showed a normal karyotype (46,XX).

Figure 1 General body view with the main ultrasonographic features: (1) encephalocele, (2) laryngeal atresia, and (3) limb anomalies. Note the dilated trachea resulting from laryngeal atresia. The heart is compressed by the bright and distended lungs (Lu).

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The fetus weighed 615 g and was hydropic (fig 1). A detailed necropsy confirmed the pre-natal findings. There was an anterior encephalocele herniating through a very large bony defect involving both frontal bones and two thirds of the parietal bones. A cartilaginous plug occluded the larynx. There was bilateral radial aplasia with a short right humerus, with three metacarpals, but only two sets of phalanges, resulting in two finger hands on both sides. There was bilateral tibial aplasia and the feet had five metatarsals on the right and four on the left. Five phalanges were present on the right but only two on the left. There was syndactyly of all four toes on the right and the first two on the left. Additional findings included short palpebral fissures and an enlarged pancreas with an increased number of islet cells. Gross examination of the brain showed an unlayered cortex suggesting agyria. However, this could not be confirmed as poor tissue preservation precluded accurate interpretation of the histological brain architecture.

Discussion

The fetus had a spectrum of malformations in which three distinct developmental fields, the upper airway, the central nervous system, and the limbs, were affected. Bilateral radial/tibial aplasia is a well defined malformation seen in many genetic disorders.² However, laryngeal atresia and an anterior encephalocele are both extremely rare anomalies.

Several possible diagnoses were considered in our case, Fraser syndrome, frontonasal dysplasia, and Mohr-Majewski syndrome (table 1). However, in all cases there were significant differences making these diagnoses unlikely.

Another possible aetiology is amniotic band disruption which has been reported in both encephalocele and limb abnormalities.³ However, this is very unlikely for several reasons. Neither ultrasound nor pathological examination showed evidence of abnormal amniotic band formation. In cases where bands are thought to be the cause of limb anomalies, the abnormality is usually one of transverse or amputation defects,² whereas in our case there were rudimentary limbs, with syndactyly and shortening.

In 1987, Machin *et al*¹ described a fetus with a similar range of anomalies, including laryngeal atresia, an asymmetrical left midparietal encephalocele, and limb anomalies (see table 1). The features described in this case are very similar to those we describe, although limb abnormalities were less severe and no renal abnormality was found in our case, whereas in the case described by Machin *et al*¹ there was a horseshoe kidney.

Laryngeal atresia is a very rare congenital malformation that is incompatible with life. In cases of complete obstruction, lung liquid accumulates within the lungs resulting in a clinical entity that has been termed congenital high airway obstruction syndrome (CHAOS).⁴ Ultrasonographic features in affected fetuses are characteristic and include bilateral, enlarged, echogenic fetal lungs together with dilated airways distal to the larynx, ascites with or without hydrops, and a small, compressed heart. Prenatal confirmation of laryngeal atresia is possible by direct visualisation of the obstructed larynx.⁵ However, the major differential diagnosis is bilateral congenital cystic adenomatoid malformation type II or III,

Table 1 Comparison of findings with the previous published cases and with published syndromes with a similar pattern of malformations

Findings	Present case	Machin <i>et al</i> ¹	Cryptophthalmos-syndactyly syndrome (Fraser)	Frontonasal dysplasia sequence	Orofaciodigital syndrome type IV (Mohr-Majewski)
Laryngeal atresia	+	+	+	–	–
Encephalocele	+	+	–	+	–
Midline facial cleft	+	–	–	+	+
Agyria	(?)	–	–	–	+
Short palpebral fissure/cryptophthalmos	+	–	+	–	–
Absent radius	Bilateral	Flexion deformities of wrist (?)	–	–	–
Absent tibia	Bilateral	Flexion deformities of hips (?)	–	–	–
Fingers	Bilateral 2 finger hand	Bilateral syndactyly	+	–	+
Toes	Bilateral syndactyly	Bilateral camptodactyly	+	–	+
Genitourinary malformations	–	Horseshoe kidney	+	–	+

which was considered as a working diagnosis in several reported cases of laryngeal atresia.^{6,7} In this regard, another case with some manifestations in common with the case described here and that of Machin *et al*¹ was recently reported.⁸ This case had an anterior encephalocele with type II congenital adenomatoid cystic malformation. The structure of the larynx was not described, but this may represent a further case.

The underlying mechanisms involved in these cases are unclear. Machin *et al*¹ suggested that lung fluid accumulation secondary to laryngeal atresia resulted in raised intrathoracic pressure, which may have been transmitted to the cranium and have led to the “expulsion” of the encephalocele. No explanation was given for the associated limb anomalies, although if the marked abdominal and thoracic distension were to cause disruption of vascular flow to the limbs this could result in the anomalies seen. This would accord with previous observations in subjects in whom “prune belly” syndrome coexisted with abnormal development of the lower extremities, such as unilateral or generalised hypoplasia.⁹ However, this seems an unlikely explanation, as, if true, one would expect to see the combination of limb anomalies and laryngeal atresia or other conditions causing increased thoracic pressure (such as pleural effusions) more frequently. Furthermore, the pattern of limb anomalies is not what would be expected secondary to vascular impairment.

In conclusion, given the obvious similarities between our case and the case published by Machin *et al*,¹ we propose that the combination of laryngeal atresia, anterior encephalocele, and limb anomalies may represent a recognisable, albeit rare, spectrum of anomalies. Prenatal laryngeal atresia is increasingly correctly

diagnosed since the advent of high resolution ultrasonography.⁵ We report this case in the hope that the presence of a large anterior encephalocele with limb anomalies will alert the ultrasonographer or the pathologist to examine the larynx. By doing so, further cases with this constellation of anomalies and variants of it may be recognised, thus showing that the coexistence of laryngeal atresia, encephalocele, and limbs anomalies is not coincidental.

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